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Surgery in Patients With Hemoglobin SC Disease

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While surgery is commonly required for complications related to hemoglobin SC (HbSC) disease, little is known about the perioperative complications or the indications for preoperative transfusion in this group. We describe the patient characteristics, preoperative transfusion regimens, and outcome in 92 patients with HbSC and sickle-variants undergoing elective surgery. Thirty-eight percent of the patients were transfused preoperatively. Patients transfused were more likely to have been hospitalized in the year prior to the surgery and scheduled for abdominal procedures. Abdominal and ear, nose and throat procedures were the most common surgeries in our study. The overall complication rate was 18% and sickle cell-related complications occurred in 9% of patients. In patients undergoing intra-abdominal procedures, the incidence of sickle cell-related complications was significantly higher in those patients not transfused prior to their surgery (35 vs. 0%). There were two deaths. We recommend selective use of preoperative transfusion in patients with HbSC disease undergoing surgery. Transfusion appears to be beneficial in abdominal cases but is not necessary with minor procedures such as myringotomy. Am. J. Hematol. 57:101–108, 1998. © 1998 Wiley-Liss, Inc.

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INTRODUCTION

Patients with hemoglobin SC (HbSC) disease frequently require surgery for complications related to their illness. High rates of perioperative morbidity and mortality have been documented in patients with homozygous hemoglobin S (HbSS) disease, but the frequency of these complications is unclear in patients with HbSC disease. Overall, patients with HbSC disease have a milder clinical course with the onset of symptoms occurring later [1] and a median survival of 60 years compared with 40 years of age in patients with HbSS disease [2]. Despite fewer episodes of acute chest syndrome (ACS) and vaso-occlusive crisis (VOC) [3,4], the incidence of avascular necrosis, retinopathy, and pregnancy-related complications is high in patients with HbSC [5–7]. Also, there is marked variability in disease severity and some patients with HbSC disease have as many complications as those patients with HbSS disease [7–11].

Reports of surgery in sickle cell patients have included only small numbers of patients with HbSC disease. While morbidity and mortality rates vary greatly in these studies, there has been no clear association between post-

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Members of the Preoperative Transfusion in Sickle Cell Disease Study Group are listed in the Appendix.

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operative complications and the type of surgical procedure, perioperative management, or transfusion therapy. As a result, there is still no agreed-upon approach to the perioperative management of these patients.

From 1988 to 1993, the multi-institutional Preoperative Transfusion Study Group randomized 604 patients with HbSS or hemoglobin sickle-beta^0 (HbSβ^0) to receive either aggressive or conservative transfusion therapy prior to elective surgery [12]. As part of this study, data were prospectively collected on 92 surgical procedures in patients with HbSC and other sickle hemoglobinopathies. Patients received standardized perioperative therapy, and data were collected during the preoperative, intraoperative, and postoperative periods. These patients, however, were not randomized to a preoperative transfusion regimen and transfusion was at the discretion of the attending physician. This report summarizes the patient characteristics, perioperative management, transfusion practices, and outcome of the patients with HbSC. Patients with HbSβ^+, HbS/HPFH, HbS/Lepore, and HbS/O-Arab, are also included.

METHODS

As part of the multi-institutional Preoperative Transfusion Study Group [12], patients with HbSC disease and other non-homozygous sickle hemoglobinopathies undergoing elective surgery were prospectively enrolled after informed consent from 28 centers. A standardized perioperative treatment protocol was followed, which included preoperative hydration; extensive intraoperative monitoring, warming, and oxygenation; as well as postoperative hydration, analgesia, oxygen administration, and incentive spirometry. Preoperative transfusion was at the discretion of the attending physician. Data collected included medical history, laboratory information, American Society of Anesthesiologist (ASA) physical status scores [13,14], Procedure Risk Category [15], and perioperative complications.

Complications were graded and specifically defined. A postoperative fever was a temperature elevation greater than or equal to 38.5°C and lasting at least 48 h. Acute chest syndrome was a new pulmonary infiltrate on a chest X-ray (CXR) involving at least one full segment, and thus did not include transient atelectasis. Pain lasting longer than 24 h, requiring narcotic analgesia, and thought to be secondary to sickling was considered a VOC. Acute chest syndrome and VOC episodes were analyzed in detail as ''sickle cell events.'' Only serious complications that prolonged hospitalization are reported here.

Data were collected on 92 surgical procedures in 88 patients. Four patients underwent two surgical procedures during the course of the study and their recent medical histories, preoperative laboratory data, surgical risk scores, and procedures were analyzed as unique patients.

TABLE I. Clinical and Laboratory Characteristics

Sex	
Female	42/92 (46%)
Male	50/92 (54%)
Age (years)	
0–9	36/92 (39%)
10–19	18/92 (20%)
20+	38/92 (41%)
Past medical history	
Asthma	4/92 (4%)
Smoking	14/91 (15%)
Hypertension	7/92 (8%)
CNS disease	7/92 (8%)
Alloimmunization	8/92 (9%)
Hospitalization within past year	55/92 (60%)
ACS within past year	6/92 (7%)
Preop screening labs	
Hypoxia	0/50 (0%)
Abnormal CXR	8/62 (13%)

To compare patient characteristics and complication rates, chi-square or Fischer exact tests for proportions were used, confidence intervals were two-sided, and a P value of 0.05 or less was considered to indicate statistical significance.

RESULTS

Patient Population

Of the patients enrolled, 75 had HbSC disease, 11 had HbSβ^+, and 6 had other sickle hemoglobin variants (HbS/HPFH, HbS/Lepore, and HbS/O-Arab). The age and sex distribution of the patients are shown in Table I. Fifty-four percent of the patients were male and 46% were female. The average age of the patients in the study was 21 years, although 39% were under the age of 10 years. In the year prior to surgery, 60% had been hospitalized and 11% had an episode of ACS. A history of central nervous system (CNS) disease was documented in 8% of the patients at study registration. All seven patients with a history of hypertension were over the age of 20 years: three had diabetes, two had congestive heart failure, one had end-stage renal disease, and one had a previous stroke. Nine percent of patients were alloimmunized at entry into the study.

Thirteen percent of the preoperative CXR's obtained were read as abnormal. (Mild cardiomegaly without pulmonary congestion was not considered abnormal in this patient population.) However, none of the patients had evidence of hypoxia, defined as room air PaO_2 less than 65, or pulse oximetry less than 92%.

Preoperative Transfusion

The average hemoglobin at study entry was 11.0 g/dl. Thirty-five of the patients (38%) were then transfused; and of these, 60% underwent exchange transfusion. The

TABLE II. Clinical and Surgical Data as Predictors for Preoperative Transfusion†

		N	% Transf.[a]
Sex			
Female		12/42	(29)
Male		23/50	(46)
Age (years)			
0–9		13/36	(36)
10–19		10/18	(56)
20+		12/38	(32)
Past medical history			
Hx of ACS	Yes	3/6	(50)
	No	32/86	(37)
Hx of asthma	Yes	3/4	(75)
	No	32/88	(36)
Hx of CNS disease	Yes	2/7	(29)
	No	33/85	(39)
Hospitalized last year	Yes	26/55	(47)*
	No	9/37	(24)
Hypertension	Yes	3/7	(43)
	No	32/85	(38)
Alloimmunization	Yes	3/8	(38)
	No	32/84	(38)
Surgical categories			
Abdominal		18/34	(53)**
E.N.T.		8/25	(32)
Orthopedic		6/11	(55)
Eye		3/11	(27)
Surgical risk			
1		8/29	(28)
2		27/63	(43)
Initial hemoglobin			
< 9 g/dl		3/4	(75)
9–11 g/dl		13/24	(54)
> 11 g/dl		16/39	(41)

†Total patients transfused = 35.
[a]Percent of patients with a particular clinical attribute that were transfused preoperatively.
*$P = 0.03$.
**$P = 0.02$.

hemoglobin concentration at study entry in the transfused patients was not significantly different from the non-transfused patients. Also, the initial hemoglobin concentrations did not differ significantly between patients who then underwent exchange transfusions compared to those who underwent simple transfusions. The preoperative hemoglobin in the transfused patients was 12.0 g/dl and did not differ significantly in the patients having undergone exchange transfusion compared to those having undergone simple transfusion. The preoperative percent HbA in the exchange group was 50% compared to 35% in the simple transfusion group ($P = 0.06$).

Potential predictors of preoperative transfusion are shown in Table II. Patients who were hospitalized within the year prior to surgery were more likely to undergo transfusion than those who had not (47 vs. 24%, $P = 0.03$). Also, patients scheduled to undergo abdominal procedures were more likely to be transfused than those undergoing other procedures (52 vs. 29%, $P = 0.02$).

TABLE III. Surgical Procedures in HbSC Patients

	No.	(%)
E.N.T.	25	(27)
Cholecystectomy	17	(19)
Splenectomy	11	(12)
Orthopedic	11	(12)
Eye surgery	11	(12)
G.U.	5	(6)
G.I.	4	(4)
Ob-Gyn	4	(4)
Vascular port	2	(2)
Craniotomy	1	(1)
Biopsy	1	(1)
Total	92	(100)

	Surgical risk categories by age	
Age (years)	Low risk (Risk = 1)	Moderate risk (Risk = 2)
0–9	14	21
10–19	5	14
20+	10	28
Total	29 (31%)	63 (68%)

Surgical Procedures and Perioperative Management

The distribution of surgical procedures is shown in Table III. Thirty-four of the procedures (38%) were intra-abdominal surgeries including cholecystectomy, splenectomy, cesarian section, exploratory laparotomy, Nissen Fundoplication, vagotomy, and abdominal hysterectomy. Twenty-seven percent of the surgeries were ENT procedures. Orthopedic and ophthalmologic surgeries occurred with the same frequency (12%). Overall, two-thirds of the surgeries were given a surgical risk score of two.

Eighty-four percent of patients were hydrated prior to their procedure. Eighty-eight percent of all surgeries were done under general anesthesia, which included intravenous narcotic in the majority of patients. In addition, epidural catheters were placed for postoperative pain management in three patients and intercostal blocks were used at the end of surgery in another two patients. Ninety-five percent of patients received postoperative hydration.

Complications

Overview. Seventeen of the patients (18%) developed at least one complication (Table IV). There was no significant difference in the overall complication rate between patients transfused preoperatively compared to those not transfused: 20 vs. 18%, respectively. However, sickle cell-related complications (ACS or VOC) occurred in 9% of patients and was higher, although not statistically significant, in the non-transfused group (12 vs. 3%, $P = 0.12$). In the transfused group, the mean preoperative Hb of those patients who developed any complication was higher, but not statistically different, than in those who did not develop complications. There were no new antibody formations or transfusion reactions noted.

TABLE IV. Postoperative Complications

	No. of patients	% of 92 cases
Fever	8	9
ACS	5	5
VOC	3	3
Miscellaneous	2	2
Death	2	2
Any post-op complication	17	18

TABLE V. Postoperative Complications and Preoperative Transfusion by Surgical Risk Score

	Risk 1 (low risk)		Risk 2 (moderate risk)	
	Transfused (N = 8)	Not Transfused (N = 22)	Transfused (N = 27)	Not Transfused (N = 35)
Sickle-cell complications	1 (13%)	0 (0%)	0 (0%)	7 (20%)*
Total complications	2 (25%)	1 (9%)	5 (19%)	9 (26%)

*$P = 0.014$.

When analyzing complication rates by surgical risk score (Table V), the rate of sickle cell disease-related events was significantly higher after moderate risk surgeries (risk score = 2) in the non-transfused group (20 vs. 0%, $P = 0.014$). Specifically, sickle cell disease events were more common after abdominal procedures than other procedures (18 vs. 3%, $P = 0.02$); and of those patients who were not transfused prior to abdominal procedures, 35% developed a sickle cell event compared to 0% in those who were transfused ($P = 0.009$). All five episodes of ACS occurred in patients who underwent intra-abdominal procedures without preoperative transfusion ($P = 0.006$). Although four of these patients had been hospitalized within the year prior to surgery, only one patient had a recent episode of ACS.

Complication and surgical subtype. Complication rates for specific surgical procedures are summarized in Table VI and described in detail for the most common surgeries.

ENT. Twenty-five patients had an ENT surgery. The majority were tonsillectomies and myringotomies. The average age of the patients undergoing ENT procedures was 8 years but the median age was 5 years. Sixty percent of these procedures received a risk score of 2 and 40% received a risk score of 1. All of these procedures were done under general anesthesia. There were three complications in these 25 patients. One patient died after a pharyngeal flap procedure secondary to airway compromise in the immediate postoperative period (see description in Deaths below). Two other patients developed prolonged postoperative fever. The average hospital stay was 3 days.

Cholecystectomy. Seventeen patients underwent cholecystectomy. The average age of the cholecystectomy patients was 25 years. Symptomatic cholelithiasis was documented in 82% of these patients. Forty-one percent of the cholecystectomies were done by the laparoscopic approach. Fifty-seven percent of the these and 50% of the open cholecystectomies were combined with other surgical procedures. Fifty-seven percent of the laparoscopic group and 40% of the open group were transfused prior to surgery.

Three patients (18%) developed postoperative complications after open cholecystectomy. The first patient was a 23-year-old with extensive past medical history who developed postoperative bleeding immediately after surgery and went on to develop ACS on postoperative day two. The second patient was a 50-year-old also with an extensive past medical history who developed ACS on postoperative day three. He then required an exploratory laparotomy and splenectomy for intra-abdominal bleeding on postoperative day twelve. The third patient developed a prolonged postoperative fever. None of these three patients were transfused in the preoperative period. No complications were described after the laparoscopic procedures. The average length of stay was 9 days for both the open and the laparoscopic patients, but the median stay for the patients undergoing laparoscopic technique was 3 days compared to 6 days for open cholecystectomy.

Splenectomy. Eleven patients underwent splenectomy. The average age was 16 years with a median age of 8 years. All patients had splenomegaly. The indication for surgery was a history of splenic sequestration or hypersplenism in 8 patients, recurrent left upper quadrant pain in 2 patients, and splenic abscess in one. Seventy-three percent of patients were transfused preoperatively. Three of the patients (27%) had a postoperative complication. One 4-year-old female, who had an episode of ACS in the year prior to surgery, was not transfused prior to surgery and she developed ACS on the fourth postoperative day. A VOC involving the extremities developed on postoperative day two in a 20-year-old. This patient also was not transfused preoperatively. The third patient developed a prolonged fever on the second postoperative day and had received a preoperative exchange transfusion. The average hospital stay was 9 days.

Eye surgery. Eleven patients underwent eye surgery. The average age of these patients was 30 years and all but one of these patients were over age 20 years. The most common procedure was vitrectomy and the majority of the procedures were done under general anesthesia. There was only one complication: a 31-year-old male was readmitted on the fifth postoperative day for a VOC. This patient did receive a simple transfusion prior to surgery. The average hospital stay for this group was 3 days.

Orthopedic procedures. Eleven patients underwent orthopedic procedures. Five patients had hip surgery (3 hip

TABLE VI. Surgical Complications by Surgery Subtype

	E.N.T. (n = 25)	Cholecystectomy (n = 17)	Splenectomy (n = 11)	Orthopedic (n = 11)	Ophthalmic (n = 11)
Average age	8	25	16	26	30
Pre-op transfusion (%)	32	47	73	55	27
General anesthetic (%)	100	100	100	73	73
Total postoperative complications (%)	12	18	27	18	9
Sickle events (%)	0	12	18	9	9
Average hospital stay (range)	3 days (1–7)	9 days (2–36)	9 days (4–17)	8 days (1–34)	3 days (1–10)

corings, 1 hip replacement, and 1 hip revision). The remaining procedures included tendon lengthening, laminoplasty, elbow arthrotomy, and a carpal-tunnel release. The average age was 26 years with a median of 32 years. Fifty-five percent of the patients were transfused prior to surgery and 73% underwent general anesthesia. There were two postoperative complications in this group. A 37-year-old patient developed VOC 2 days after a hip revision. Another patient developed a prolonged postoperative fever after a total hip replacement. The average hospital stay was 8 days with a median admission of 4 days.

Deaths. Two patients (2%) died during the study. The first patient, a 35-year-old pregnant woman with HbSC disease, was admitted for VOC involving her legs. She had undergone two previous C-sections. Three days after admission she underwent a C-section for fetal bradycardia. Her preoperative physical exam was remarkable only for poor dentition. Her hemoglobin was 10.0 g/dl and she was not transfused prior to the surgery. A 50% abruption was diagnosed at delivery. Respiratory distress was noted the following day and she went on to develop respiratory failure. She expired on postoperative day four. Autopsy data were unavailable.

The second patient, a 15-year-old with HbSβ^+, was admitted for elective pharyngeal flap for correction of her hypernasality of speech. She had a left complete cleft palate diagnosed at birth and had undergone primary repairs without difficulties. Her preoperative hemoglobin was 11.4 g/dl. The procedure was uncomplicated and she was extubated in the operating room. She was coughing and lifting her head from the table, but after arrival to the recovery room, she was unresponsive, pupils were fixed and dilated, and had no effective respiratory efforts. She required ventilatory and inotropic support in the intensive care unit. She developed signs of diabetes insipidus, developed electro-mechanical dissociation, and expired on postoperative day two. Autopsy revealed diffuse pneumonia, pulmonary congestion, and diffuse cerebral hypoxic injury. The cause of death was attributed to the hypoxic brain injury.

DISCUSSION

Recommendations for the perioperative management of patients with sickle cell disease vary widely. It is agreed upon that patients should be warmed, well hydrated, well oxygenated and mildly alkalotic to avoid conditions that could lead to relative or regional hypoxia, increase sickling, and compromised oxygen delivery to tissues [16–22]. While there may be theoretical advantages of regional anesthesia over general regimens, compensatory vasoconstriction may occur in unanesthetized areas during regional anesthesia [23], and there is even limited evidence that sickling may be temporarily reduced during general anesthesia [24]. Most authors recommend choosing the anesthetic regimen most appropriate for the surgical procedure [18,21]. In this study, we report the outcome of 92 elective surgical procedures in patients with HbSC disease and other sickle hemoglobinopathies. Despite standard perioperative care, the overall complication rate was 18% and the rate of specific sickle cell events was 9%. Intra-abdominal surgeries were associated with the highest rate of morbidity, especially in patients that were not transfused preoperatively.

In this report, we demonstrate a significantly lower rate of complications in those patients transfused prior to abdominal procedures, even though patients transfused tended to be more frequently admitted for complications relating to their illness. Abdominal procedures are known to be associated with significant postoperative pain, which can lead to respiratory splinting, segmental hypoxia, and predispose a patient to a micro environment that increases sickling. Preoperative transfusion, by lowering the percentage of sickle cells, should prevent some of the complications listed above. Of those patients undergoing abdominal procedures, no sickle cell-related complications were seen in patients transfused preoperatively, whereas 35% of those not transfused developed ACS or VOC. While the HbSC disease patients in our study were not randomized to preoperative transfusion groups, a similar increase in complications was noted in HbSS disease patients undergoing cholecystectomy without preoperative transfusion [25].

There is no consensus on the indications for, or the type of, preoperative transfusion in HbSC disease. While transfusion therapy has been shown to increase the oxygen-carrying capacity and decrease viscosity associated with sickling [26,27], there are numerous associated risks including infection, transfusion reactions, decreased immunocompetency, and alloimmunization [12,28,29]. Most other studies of surgery in sickle cell disease have been retrospective and difficult to compare because of the variability in preoperative transfusion regimens, surgical procedures, and perioperative management [17,30–41]. A few of these studies included only a small number of HbSC disease patients. In the Cooperative Study of Sickle Cell Disease, a retrospective review of surgical procedures in 102 patients with HbSC disease was included, although detailed past medical history and perioperative management guidelines were not discussed [42]. Preoperative transfusion occurred in 54% of the procedures and was shown to be beneficial in lowering the rate of sickle cell-related complications in both low- and moderate-risk surgeries. In our study, preoperative transfusion was a benefit only in moderate-risk surgeries. We have previously shown that conservative preoperative transfusion is as effective as aggressive transfusion in HbSS disease patients [12]. However, as patients were not randomized to a preoperative transfusion regimen, and only one sickle cell-related complication occurred in the transfused patients in our study of HbSC disease, we are unable to effectively compare exchange transfusion to conservative regimens in this group. Furthermore, the sample size and complication rate in this study may not be sufficient to evaluate the relationship of viscosity and postoperative complications.

The overall complication rate in our study was 18%, substantially lower than seen in HbSS disease patients in the Preoperative Transfusion Study [12,25]; however, the mortality rate (2%) was slightly higher. There are other reports of postoperative death in HbSC disease patients after a variety of surgical procedures [42–46]. Acute chest syndrome is a common cause of death in sickle cell disease and preceded the death of the 35-year-old following cesarian section in this study. The other death in our study was secondary to immediate postoperative hypoxia.

CONCLUSION

In conclusion, we demonstrated a total postoperative complication rate of 18% in HbSC disease patients undergoing elective surgical procedures. Nine percent of patients developed ACS or VOC. The occurrence of these sickle cell events was significantly higher after abdominal surgery especially in patients that were not transfused preoperatively (35 vs. 0%). Based on this and our previous reports in patients with HbSS disease [12,25], we would recommend preoperative transfusion for HbSC disease patients undergoing intra-abdominal procedures. Exchange transfusion may be required to keep hemoglobin levels less than 12 and to avoid the potential problems associated with hyperviscosity. Patients undergoing low-risk procedures may not require preoperative transfusion unless they have had significant complications related to their disease. We also recommend that HbSC disease patients receive preoperative hydration; extensive intraoperative monitoring, warming, and oxygenation; and postoperative hydration, oxygen administration, incentive spirometry, and appropriate pain management.

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APPENDIX

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